Radionuclide Quantitation of Right-to-left Intracardiac Shunts in Children

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SUMMARY A simple, noninvasive method for measurement of right-to-left intracardiac shunts would enhance the management of patients with congenital heart disease. This study describes application of data processing techniques used previously in dye-indicator curves to data recorded during the initial transit of radioactive bolus through the central circulation. Radionuclide angiograms were performed in 20 children, mean age 30 months, immediately after cardiac catheterization for congenital heart disease. The radionuclide data recorded over the carotid artery were used to replace arterial sampling required for dye indicators, and forward triangles were fitted to calculate the right-to-left shunt in an approach similar to that of Wood for indicator-dilution curves. Ten of the children had right-to-left shunts by Fick and radionuclide measurement, and 10 of the children with septal defects had no right-to-left shunt by either technique. Both the radionuclide and Fick measurements correlated well (r = 0.95). Therefore, radionuclide angiographic data may be used for accurate calculation of right-to-left shunts in small children, eliminating the need for arterial sampling.

A NONINVASIVE procedure for diagnosis and quantitation of right-to-left intracardiac shunts could aid the differentiation of pulmonary and cardiac causes of cyanosis in the neonate and provide objective documentation of change in shunt size in older children with cyanotic heart disease. Indicator-dilution curves obtained with i.v. injection and arterial sampling of dye permit right-to-left shunt quantitation, but the arterial puncture and blood withdrawal required entail some risk in young children and cannot be routinely performed on an outpatient basis. The radionuclide techniques previously advocated for measurement of right-to-left intracardiac shunts have required either arterial sampling or i.v. injection of labeled particles. Radionuclide angiography is becoming widely used in children to measure left-to-right intracardiac shunts and to assess left ventricular function. Images obtained from the movement of the tracer bolus through the heart have been used to depict right-to-left shunts, but no technique for shunt quantitation has been devised. The purpose of this investigation was to develop a technique for processing radionuclide angiographic data to accurately measure right-to-left intracardiac shunts.

Methods

Study Design

Twenty children with a congenital heart disorder associated with an atrial or ventricular septal defect (ASD and VSD) underwent cardiac catheterization and radionuclide angiography. The children were 6–61 months of age (mean 30 ± 18 months). Thirteen were boys and seven girls. The clinical
diagnosis before catheterization was VSD in seven, ASD in three and tetralogy of Fallot in five. One patient had double-outlet right ventricle with VSD and a previous pulmonary artery band, one had a VSD with pulmonary hypertension, one had pulmonary atresia, one had tricuspid atresia and one had transposition of the great vessels. Clinical cyanosis was present in seven of the 20 children before catheterization, but each of the children had a clinical diagnosis that might have been associated with right-to-left intracardiac shunting.

The children were sedated with 2 mg/kg of Demerol and 1 mg/kg of Phenergan for cardiac catheterization, which was performed by a standard technique. At the time of catheterization, blood was sampled from the superior and inferior vena cavae, pulmonary veins and thoracic aorta. Mixed venous saturation was derived as one-third of superior vena cava saturation plus two-thirds inferior vena cava saturation. Saturation was measured in blood sampled from one right and one left pulmonary vein and averaged to obtain the pulmonary venous saturation. The right-to-left intracardiac shunt was quantitated by the Fick principle using the equation:

\[
\text{right-to-left shunt} = \frac{\text{PVO}_2 - \text{SAO}_2}{\text{PVO}_2 - \text{MVO}_2},
\]

where \( \text{O}_2 \) = oxygen saturation, \( \text{PV} \) = pulmonary vein, \( \text{SA} \) = systemic artery and \( \text{MV} \) = mixed venous blood. Pressures were measured in all cardiac chambers, and the contrast angiograms necessary for clinical management of the children were obtained.

Immediately after catheterization, the catheter used to examine the right heart was withdrawn into the inferior vena cava and used for radionuclide injection. Technetium-99m pertechnetate (0.3 mCi/kg with a 2-mCi minimum dose) was loaded into an extension tubing connected to the venous catheter so that a tracer bolus could be rapidly injected by a saline flush. Data were recorded from the anterior projection at 25-msec intervals for a 30-second period. A computerized multicroystal gamma camera (Baird System Seventy-Seven) equipped with a 1-inch parallel-hole collimator was used to record and process data.

Radionuclide Data Processing

Observed counts were corrected for variation in detector efficiency and electronic dead time loss of the instrument. A temporal smoothing program constructed a sliding average of data by adding one-half of the preceding and subsequent frames to each frame to minimize statistical fluctuations in the data. Images of the initial transit of tracer bolus through the central circulation were used to assign regions of interest to data recorded over the inferior vena cava, pulmonary artery, lungs, left ventricle and carotid arteries. The anatomic accuracy of the designated regions was confirmed by the indicator-dilution principle (fig. 1).

Forward triangles were fitted to the first and to the second component of the carotid time-activity curve in a manner similar to that described for processing dye indicator-dilution curves (fig. 2). The appearance time and the time of peak activity of the shunted tracer and the normally circulating tracer were computed using the time of tracer appearance in the inferior vena cava as zero. When no shunt was present, scattered radiation caused a near-constant level of counts that occurred early in the carotid curve before actual tracer flow, and no early peak could be recognized. In these patients, the triangle was positioned on the plateau at the time midway between the peak of the pulmonary artery and lung curves. The area of this small triangle was calculated as if it were a small right-to-left shunt to avoid the possibility of bias in processing data from patients with small shunts.

In patients with large right-to-left shunts, recirculation of a portion of the large quantity of shunted tracer interfered with determining the quantity of normally circulating tracer. In these patients, the second triangle on the carotid artery data was positioned to coincide with the time of maximum of the left ventricular curve.

Data Comparison

The magnitude of right-to-left shunt was independently calculated from radionuclide data by one investigator and from Fick data by another. The results of these blind calculations were then compared by linear regression analysis. The resulting equation was used to correct the radionuclide measurements, which were then subtracted from corresponding Fick measurements. The mean and standard deviation of the resulting differences were calculated as an index of variability between the two methods.
Results

Serial images of the initial tracer transit through the heart and lungs permitted selection of anatomic regions for curve generation in all children (fig. 1). Children with the largest shunts had the most marked shunt flow on these images (fig. 3).

Time-activity curves recorded from the carotid arteries in three patients are shown in figure 4. Scattered radiation causes an early, relatively constant counting rate prior to the actual levophase in patients without a right-to-left shunt. In the children with a right-to-left shunt, the early plateau is replaced by a definite increase in carotid counts and the magnitude of this increase is greatest in the child with the largest shunt.

Clinical data and shunt measurements are summarized in table 1. All the children with isolated ASD or VSD and predominant left-to-right shunting had no right-to-left shunting by oximetry data. In this group, uncorrected right-to-left shunt measurements from radionuclide data ranged from 0.02–0.14. In the children with cyanotic heart disease, right-to-left shunts calculated from the catheterization data ranged from 0.10–0.79, and shunt values calculated from radionuclide data ranged from 0.19–0.68. Measurements obtained by both techniques correlated well by linear regression analysis (r = 0.95) (fig. 5). Correction of the radionuclide shunt measurements by the regression equation resulted in an average right-to-left shunt value of 0 ± 5% (range 8–5%) in the 10 children without a right-to-left shunt by the Fick technique. The mean ± sp between the corrected radionuclide data and the Fick measurements was 0 ± 8% for all 20 children and 1 ± 10% for the 10 children with right-to-left shunts.

Discussion

Assessment of the magnitude of right-to-left shunting is frequently important in the management of the cyanotic newborn, in the timing of operative correction of congenital heart disease in older children and in the postoperative evaluation of both of these patient groups. Fick and dye-indicator methods can accurately measure right-to-left shunts, but these techniques require cardiac catheterization or arterial sampling, procedures that may be hazardous in newborn infants with cardiorespiratory distress. The purpose of this investigation was to devise a noninvasive approach for right-to-left shunt quantitation using radionuclide angiocardiography.

The first attempt to evaluate congenital heart disease using radioactive tracers was reported by Prinzmetal in 1949. A single Geiger-Muller counter was used to record appearance of precordial counts after i.v. injection of radioactive sodium in two patients with tetralogy of Fallot. In 1957, Huff et al. used four scintillation detectors positioned over different anatomic sites to evaluate patients with congenital heart disease. Greenspan et al. positioned one detector over the precordium and another over the femoral artery and measured heart–femoral artery appearance time of radioactivity. Patients with right-to-left shunting showed early appearance of tracer in the femoral artery, but no methods for shunt quantitation were attempted. Subsequent studies used individual detectors to generate time-activity curves to detect, but not quantitate, right-to-left shunts. These early single-probe techniques were limited by a prolonged tracer bolus typical of peripherally recorded data, by low counting rates and by lack of reproducible methods for detector positioning. These disadvantages were not overcome even by arterial sampling, and these techniques never attained routine clinical use.

The radioactive particle distribution method has also been used to measure right-to-left shunts. After i.v. injection, labeled macroaggregates of serum albumin are almost completely trapped in the lungs of normal subjects. In patients with right-to-left in-
tracardiac shunts, a portion of the injected material bypasses the pulmonary circulation and lodges in systemic capillaries. Therefore, comparison of systemic-to-pulmonary counts has been shown to provide an index of shunt magnitude. This approach imposes the complexities of total body counting and has the potential hazard of systemic embolization of the particles that pass through the shunt. Injection of the necessary quantity of appropriately sized particles has been documented to be safe, but strict quality control is essential to ensure that no large aggregates form in the radiopharmaceutical.

Over the past decade, radionuclide angiography using computerized gamma cameras has been developed for imaging or quantitating the transit of a tracer bolus through heart and lungs. This procedure is becoming more widely used to assess left ventricular function and to measure left-to-right shunting in children with congenital heart disease. This use has defined the need for a data processing technique that accurately measures right-to-left shunting using radionuclide angiography. We applied a principle previously described for processing dye indicator-dilution curves to radionuclide data. The results confirm that data recorded over the carotid arteries are similar to those obtained by arterial sampling. The spatial and temporal resolution of the data permitted accurate definition of the detector area that corresponded to specific anatomic regions. This approach to region-of-interest selection was essential for the accuracy of the technique.

We described the accuracy of this approach in experimental animals. Right-to-left shunting was induced in dogs with a surgically created ASD by partial occlusion of the pulmonary artery with an inflatable device. Twenty simultaneous radionuclide and indocyanine dye measurements in seven animals correlated well ($r = 0.97$).

In the present study, radionuclide measurements were compared with Fick measurements based on oxygen saturation determinations. The Fick method depends on an equilibrium state, in contrast to the radionuclide data, which reflect flow through the shunt at the actual time of tracer transit through the heart. This basic difference between the approaches might be expected to introduce some discrepancy in measurements in children with bidirectional shunting. However, both techniques agreed well, even in children with
TABLE 1. Clinical Data and Shunt Measurements in Individual Patients

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<tr>
<th>Pt</th>
<th>Age (months)</th>
<th>Sex</th>
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<th>Diagnosis</th>
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Abbreviations: M = murmur; CHF = congestive heart failure; RVH = right ventricular hypertrophy by ECG; CY = cyanosis; ASD = atrial septal defect; VSD = ventricular septal defect; PAH = pulmonary arterial hypertension; TOF = tetralogy of Fallot; DORV = double-outlet right ventricle; PA = pulmonary atresia; TA = tricuspid atresia; TOGV = transposition of the great vessels.

Predominant left-to-right shunts. The radionuclide technique also appeared to correlate with Fick measurements of the right-to-left shunt/systemic flow ratio in children with disorders that cause an actual 100% right-to-left shunt at the cardiac level, such as tricuspid or pulmonary atresia.

The y intercept of 12% on the radionuclide and Fick

**FIGURE 4.** Carotid artery time-activity curves recorded in the three children described in figure 3. The ratio of the first to the second component reflects the size of the right-to-left shunt.

**FIGURE 5.** Comparison of radionuclide and Fick measurement of right-to-left shunting in 20 children with congenital heart disease.
regression comparison reflects the area of the triangle positioned on the count plateau early in the carotid artery curve of all patients due to scattered radiation. Less bias was introduced by using the regression equation to correct the observed radionuclide shunt than in application of background-subtraction techniques. In addition, contrast echocardiographic studies reveal that a small amount of right-to-left shunting occurs in almost all patients with septal defects and predominant left-to-right shunting. The present study does not permit determination of whether the Fick or the radionuclide technique is more sensitive in detecting small right-to-left shunts.

In the present study, the radionuclide measurement was obtained immediately after cardiac catheterization. Therefore, it was more feasible to withdraw the indwelling catheter from the right heart into the inferior vena cava for tracer administration than to perform separate venipuncture for the injection. However, the clinical valve of this technique for right-to-left shunt quantitation would be limited if the measurement required a central venous injection. In previous studies in children, we found that a radionuclide injection into an antecubital or saphenous vein consistently provided data with a discrete appearance of tracer in the central circulation that would be necessary for right-to-left shunt calculation. The configuration of the tracer bolus entering the right heart should be examined using data recorded during injection. Shunt calculation should not be attempted if tracer entry into the right atrium is prolonged or erratic. In our experience, peripheral venous injections provide data that are adequate for right-to-left intracardiac shunt calculation in almost all children.

The good correlation of radionuclide and Fick data in this study emphasizes the clinical value of radionuclide angiocardiology in congenital heart disease. Important uses of the technique might include examination of cyanotic children before cardiac catheterization and the serial documentation of shunt size in older children. In addition, right-to-left shunt measurement could be combined with evaluation of right and left ventricular function using the same radionuclide injection. The simplicity of the technique is also well suited for quantitation of change in the magnitude of right-to-left shunting during exercise stress or drug interventions.

References
Radionuclide quantitation of right-to-left intracardiac shunts in children.
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